

## REMARKS

### Amendments to the Claims

With the present submission, claims 18 and 20-33 have been amended. Claim 19 has been canceled without prejudice or disclaimer. No new claim has been added. As such, claims 18 and 20-33 are currently under consideration.

In particular, claim 18 has been reworded to recite a chemically modified double stranded nucleic acid molecule having a sense strand and a separate antisense strand of the specified lengths, comprising two or more different Northern conformation chemical modifications. This amendment, however, does not change the scope of claim 18 as it was previously presented, but has been made solely to improve grammatical coherence and provide proper antecedent basis for later, dependent claims. As such, claim 18 is fully supported.

Each "siNA" has been replaced with "nucleic acid" in claims 20-33 to insure proper antecedent basis. The terms "first strand" and "second strand" have been amended to recite "sense strand" and "antisense strand," respectively, in claims 22 and 23. The terms "sense region" and "antisense region" have also been amended to recite "sense strand" and "antisense strand," respectively, in claims 28-32. A term "terminal" has been added to before "cap moiety" in each of claims 24 and 25, to insure proper antecedent basis. These amendments are made solely in form rather than in substance, thus not affecting the scope of the corresponding claims.

No new matter has been added as a result of these proposed amendments. Accordingly, Applicants respectfully request their entry.

### The Restriction Requirement

The Office alleged: (1) that the application contains claims directed to a plurality of patentably distinct species; and (2) that the species have "mutually exclusive characteristics." *See* Restriction Requirement, at page 3.

Specifically, Applicants are required to elect a double stranded molecule "with a specific pair of [Northern conformation] modifications for examination, including which strand or strands contain(s) modifications and what those modifications are." *Id.* The Office acknowledged claim 18 as the generic linking claim. Applicants hereby elect a chemically modified double stranded nucleic acid molecule wherein both the sense and the antisense strands comprise more than one modified

nucleotides having Northern conformation modifications. Applicants also elect locked nucleic acid (LNA) and 2'-O-methyl Northern conformations for initial examination. Instant claims 18 and 20-33 read on the elected species. These elections are made with traverse, however, as Applicants believe that the generic claim includes sufficiently few species that a search and examination of all the species at one time would not impose an undue burden on the Office. The alleged species are also not mutually exclusive as alleged because these molecules are fully capable of being used together, as expressly taught by the instant specification:

The nucleic acid molecules of the instant invention, individually, or **in combination** or in conjunction with other drugs, can be used to treat diseases or conditions discussed herein (e.g., cancers and othe[r] proliferative conditions, viral infection, inflammatory disease, autoimmunity, pulmonary disease, renal disease, ocular disease, etc.).

Specification, at page 85, lines 1-4 (*emphasis added*). These molecules also share a common structural motif, including comprising two separate strands, each 19 to 29 nucleotides long, with each strand having two or more different Northern conformation modifications. Moreover, these molecules also do not have materially different biological effects in terms of inhibiting gene expression, although the levels of activity may differ depending on the modification types. The Office has acknowledged claim 18 as a generic linking claim. Pursuant to MPEP 803.02, the search and examination of the elected species will be expanded to the full scope of the generic linking claim if the prior art allows. Thus, Applicants respectfully urge the early rejoinder and consideration of the non-elected species.

The Office further required election between a “chemically synthesized ds-siRNA wherein the siRNA comprises no ribonucleotides,” and a “chemically synthesized ds-siRNA wherein the siRNA comprises one or more ribonucleotides,” but acknowledged that claim 18 is generic. *See* Restriction Requirement, at page 3. It is respectfully noted that claim 19 has been canceled herein without prejudice or disclaimer, thereby rendering this restriction requirement moot. Accordingly, Applicants request withdrawal of the restriction requirement in this respect.

The Office also required the election among the molecules wherein (1) the sense strand includes a terminal cap moiety at the 5'-end, (2) the sense strand includes a terminal cap moiety at the 3'-end, and (3) the sense strand includes a terminal cap moiety at both the 5'-end and the 3'-end. *See id.* at page 4. The Office acknowledged that claim 18 is generic. Applicants hereby elect a molecule comprising a terminal cap moiety at both the 5'-end and the 3'-end for initial examination

on the merits. Claims 18 and 20-33 read on the elected species. This election, however, is made with traverse as the number of alleged species is 3, which can by no means be said to create an undue burden if the Office is to search and examine all the alleged species at one time. Moreover, the alleged species are not mutually exclusive in the sense that the alleged species are capable of being used together, share at least one common structural design, and share the same biological effects of inhibiting gene expression, as explained above. Accordingly, Applicants respectfully urge the early rejoinder of the non-elected species in accordance to the search and examination procedures of MPEP 803.02 and in view of the acknowledged generic linking claim 18.

Furthermore, the Office required the election between a molecule wherein “pyrimidine nucleotides in the sense region are 2’-O-methyl pyrimidine nucleotides,” and wherein “pyrimidine nucleotides in the sense region are 2’-deoxy-2’-fluoro pyrimidine nucleotides,” but acknowledged that instant claim 18 is generic. *See* Restriction Requirement, at pages 4-5. Applicants hereby elect a construct wherein the pyrimidine nucleotides in the sense strand are 2’-deoxy-2’-fluoro pyrimidine nucleotides for initial examination on the merits. Claims 18, 20-29, and 31-33 read on the elected species. This election is also made with traverse as the number of species is 2 in the generic claim, which will not be an undue burden to search and examine together. These allegedly separate constructs are not mutually exclusive in that they are fully capable of being used together, share at least one common structural design, and share the same biological effects of inhibiting gene expression, as explained herein. Accordingly, Applicants respectfully request withdrawal of the instant restriction requirement and early rejoinder of the non-elected species in accordance with MPEP 803.02 and in view of the fact that claim 18 is an acknowledged generic linking claim.

### **Conclusion**

In view of the foregoing, Applicants respectfully request early action on the merits. If the Examiner believes a telephone conference would expedite prosecution of this application, she is urged to telephone the undersigned at the telephone number below.

If it is believed that a teleconference will advance prosecution, the examiner is encouraged to contact the undersigned as indicated below.

Date: April 8, 2008

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Respectfully submitted,

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